Working standing is possible!
but without
"Postural Tachycardia Syndrome"

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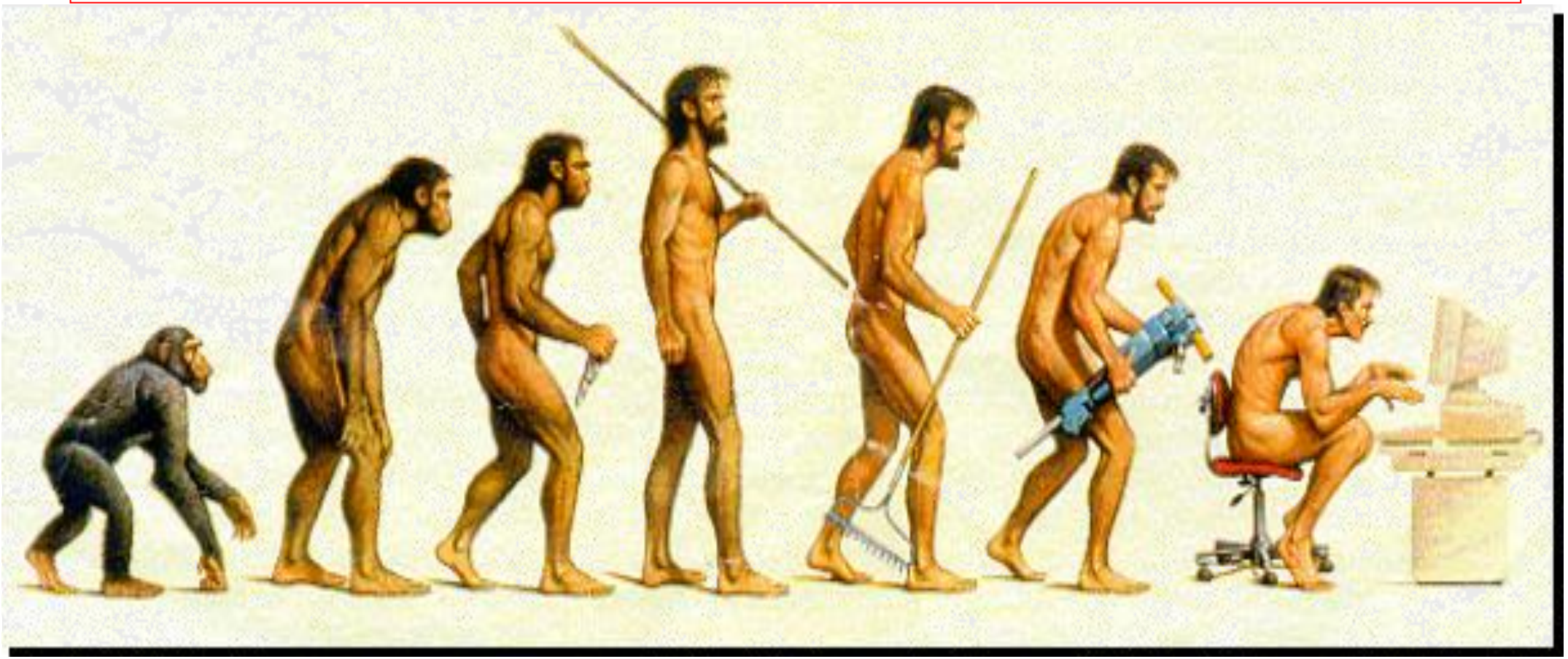
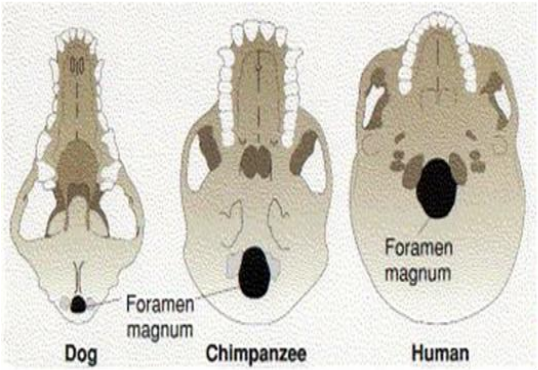
One Million Years of Evolution

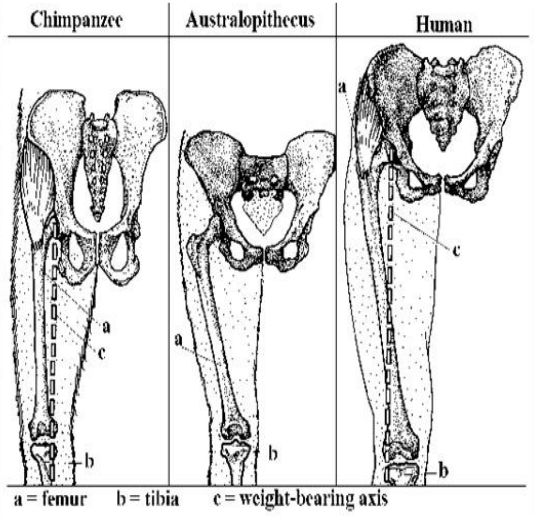


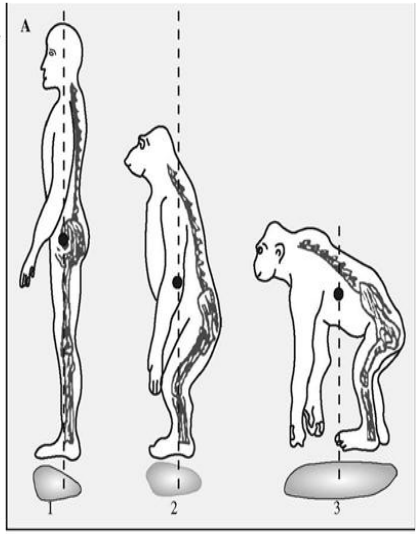
Bipedalism

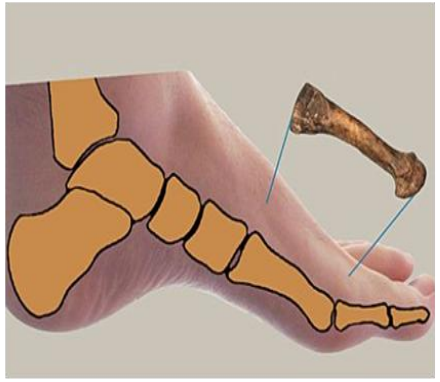
Mechanical Standing

Brain, Bone, Muscle, Joints …

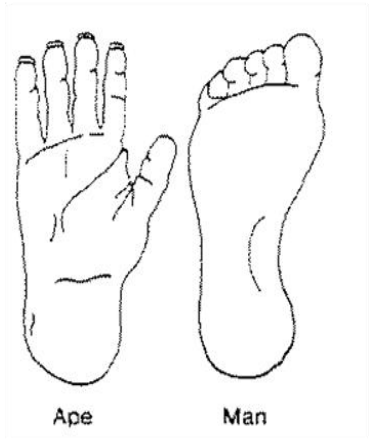


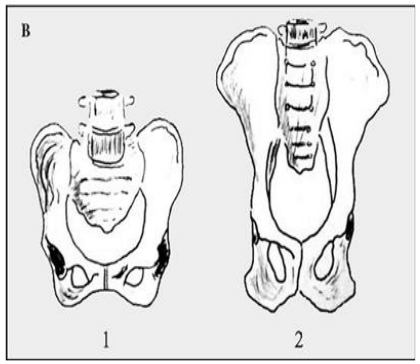


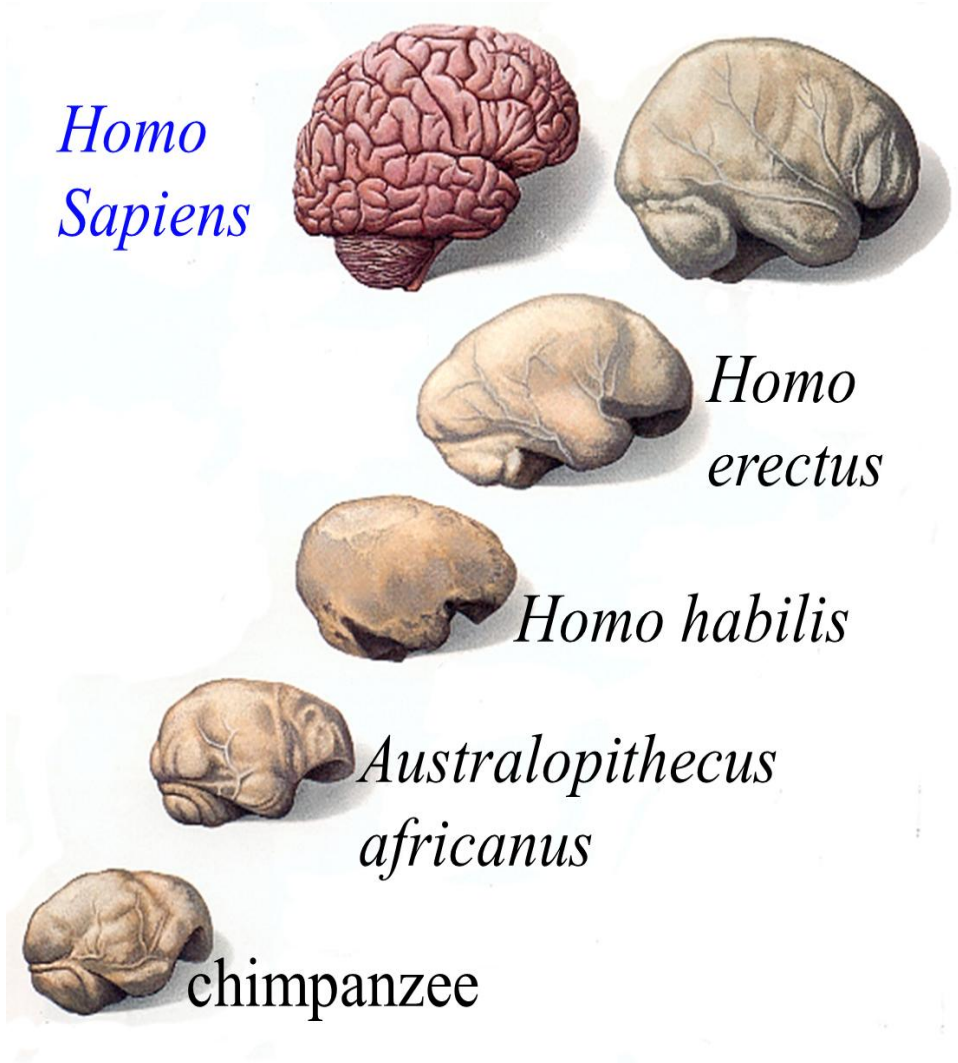




The *A. afarensis* foot bone is shown with a human foot indicating where it would be positioned.







Hemodynamic Standing "Upright Posture"

- In order to stand, we must overwhelm the gravity effects on hemodynamic (+ Mechanical Coupling)

- One million years of evolution:
  - Maintenance of blood pressure (BP)
  - Cerebral Blood Flow (CBF): Brain-O_2
  - Effective Circulating Volume (ECV)

Blood Volume Redistribution
Gravity Effects

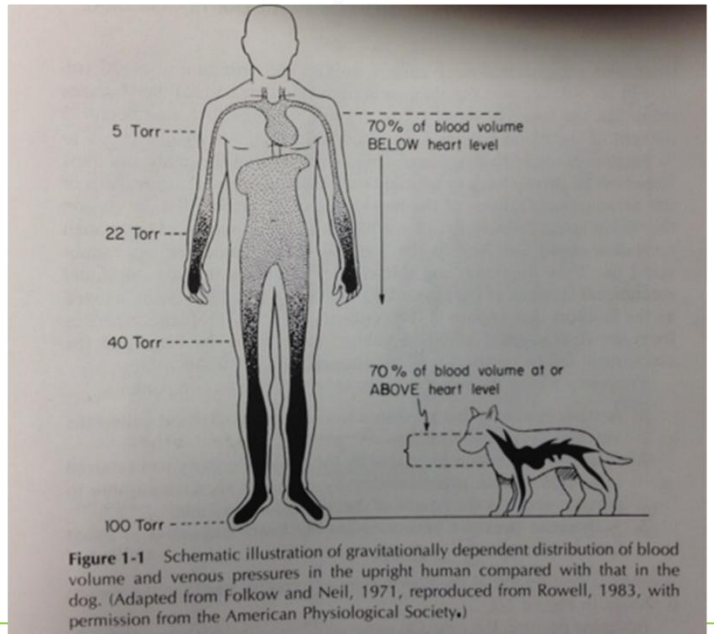


Figure 1-1 Schematic illustration of gravitationally dependent distribution of blood volume and venous pressures in the upright human compared with that in the dog. (Adapted from Folkow and Neil, 1971, reproduced from Rowell, 1983, with permission from the American Physiological Society.)

Hemodynamic Standing:

Total Peripheral Resistance = TPR

- Mean BP = CO (SV * HR) x **TPR**
- Sympathetic tone is essential (*80%* vasoconstriction)
- "Healthy" Autonomic Nervous System
  is an Requirement !!!

Autonomic Dysfunction that cause, Orthostatic Intolerance

- Constitutional Hypotension (SBP < 100 mm Hg)
- Orthostatic Hypotension
- Syncope
- Postural Tachycardia Syndrome = POTS

Constitutional Hypotension: (CHT)

Nomenclatures

- “Optimal” BP
- Chronic Hypotension
- Essential Hypotension
- Low blood pressure

- **Constitutional Hypotension**

Definition

- Systolic BP < 100 , Women
- Systolic BP < 110 , Men

WHO (1978), arterial hypertension, Technical report series # 628, World Health Organization, Geneva.

Epidemiology of CHT:

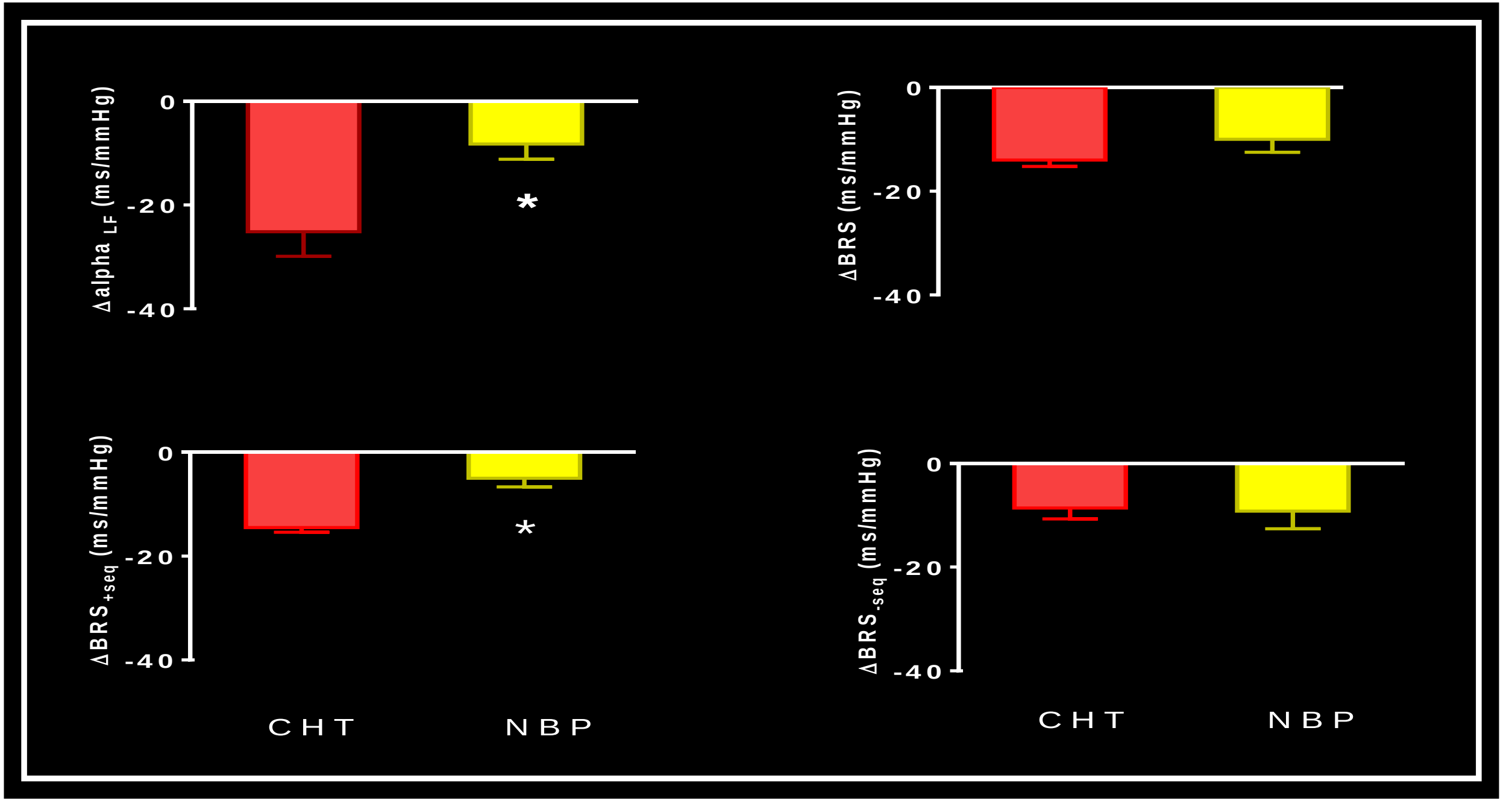
- Affects 2-4% of the adult population (German reports)
- Predominantly Women
- BMI tends to be low
- Muscle mass and serum creatinine are low
- Low cardiovascular mortality ..
- High life expectancy

Symptoms: reported by subjects with CHT

- **<u>Psycho-affective symptoms</u>**:
  - Anxiety / depression
  - Low motivation
  - Cognitive disturbance (CBF dysregulation)
  - Fatigue
  - Reduced QoL
- **<u>Hypotension related symptoms</u>**:
  - Dizziness
  - Pre-syncope and syncope
  - Chest discomfort and palpitation
  - Cold limbs (ANS)
  - Sweat disorders (ANS)
  - ***Fatigue***

Supine Power Spectral Analysis	CHT	NBP
LF_{RR}, ms^2	1115±223	525±93*
HF_{RR}, ms^2	1009±298	1062±316
Alpha-LF, ms/mmHg	39.1±4.7	20.1±2.5*
BRS, ms/mmHg	29.2±0.7	25.2±1.6*
BRS_{+seq}, ms/mmHg	27.2±0.5	16.5±1.6*
BRS_{-seq}, ms/mmHg	24.0±1.2	26.7±1.9

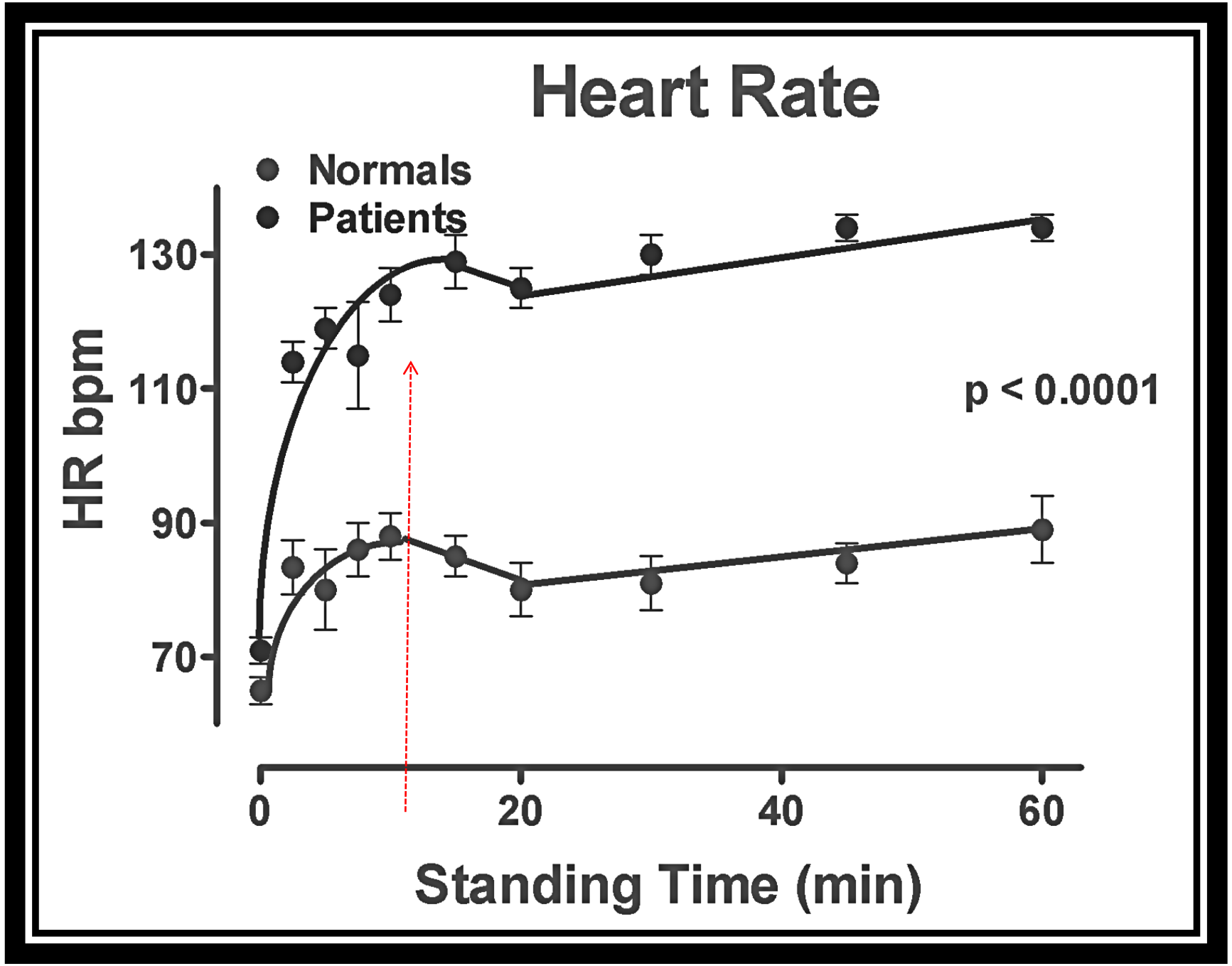
Delta HUT Baroreflex Sensitivity

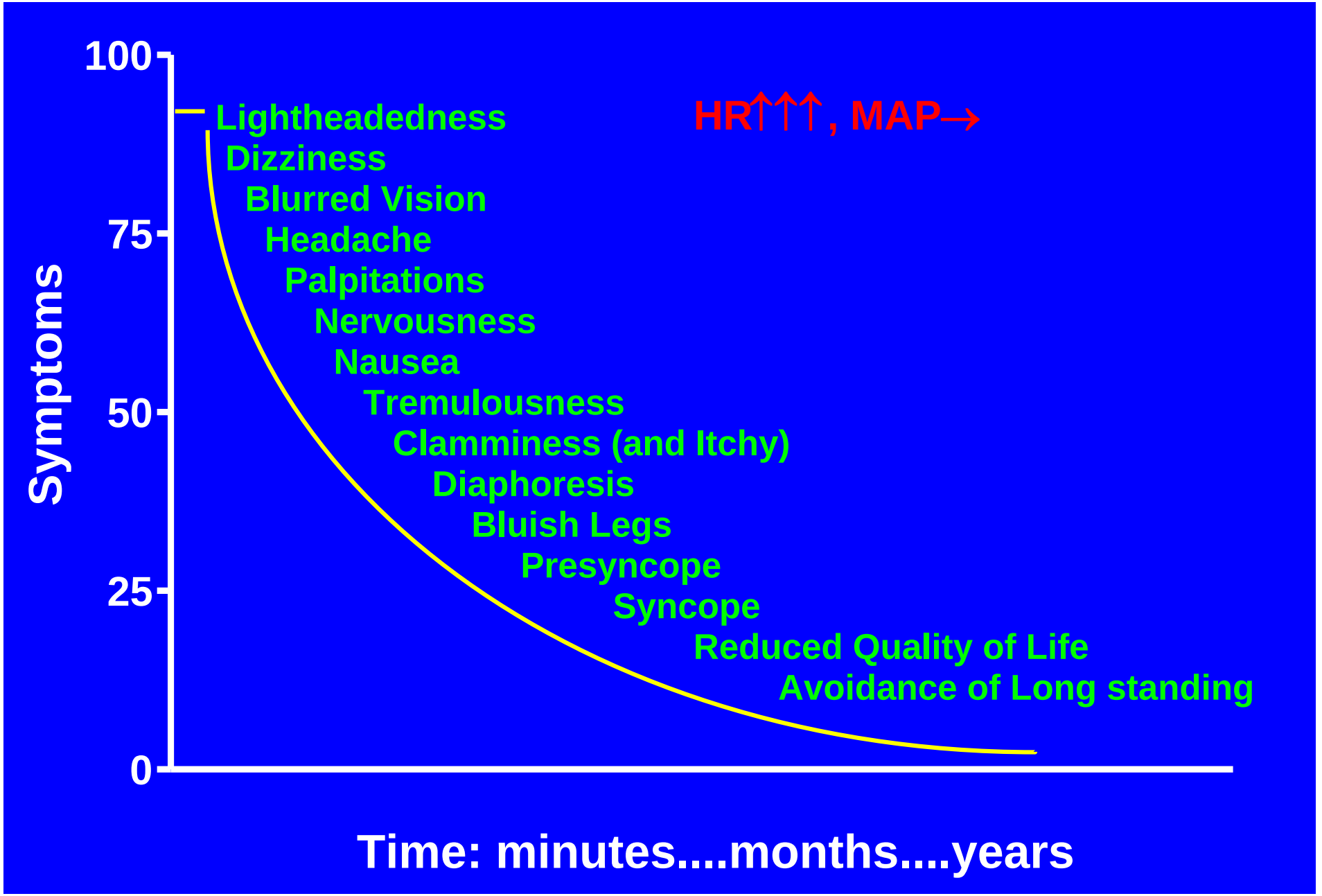


Postural Tachycardia Syndrome = POTS

- Remarkable increase in Heart Rate upon standing

  >30 bpm, (after 5-10 minutes)
- Blood Pressure unchanged (no OH), or increases
- Orthostatic Symptoms (> 4-5 symptoms) for > 6 months
- Absence of a systemic illness (Idiopathic vs. Secondary)


Heart Rate
Normals
Patients
HR bpm
130
110
90
70
p < 0.0001
0
20
40
60
Standing Time (min)


100
75
50
25
0
Symptoms
Lightheadedness
Dizziness
Blurred Vision
Headache
Palpitations
Nervousness
Nausea
Tremulousness
Clamminess (and Itchy)
Diaphoresis
Bluish Legs
Presyncope
Syncope
Reduced Quality of Life
Avoidance of Long standing
HR↑↑↑, MAP→
Time: minutes....months....years

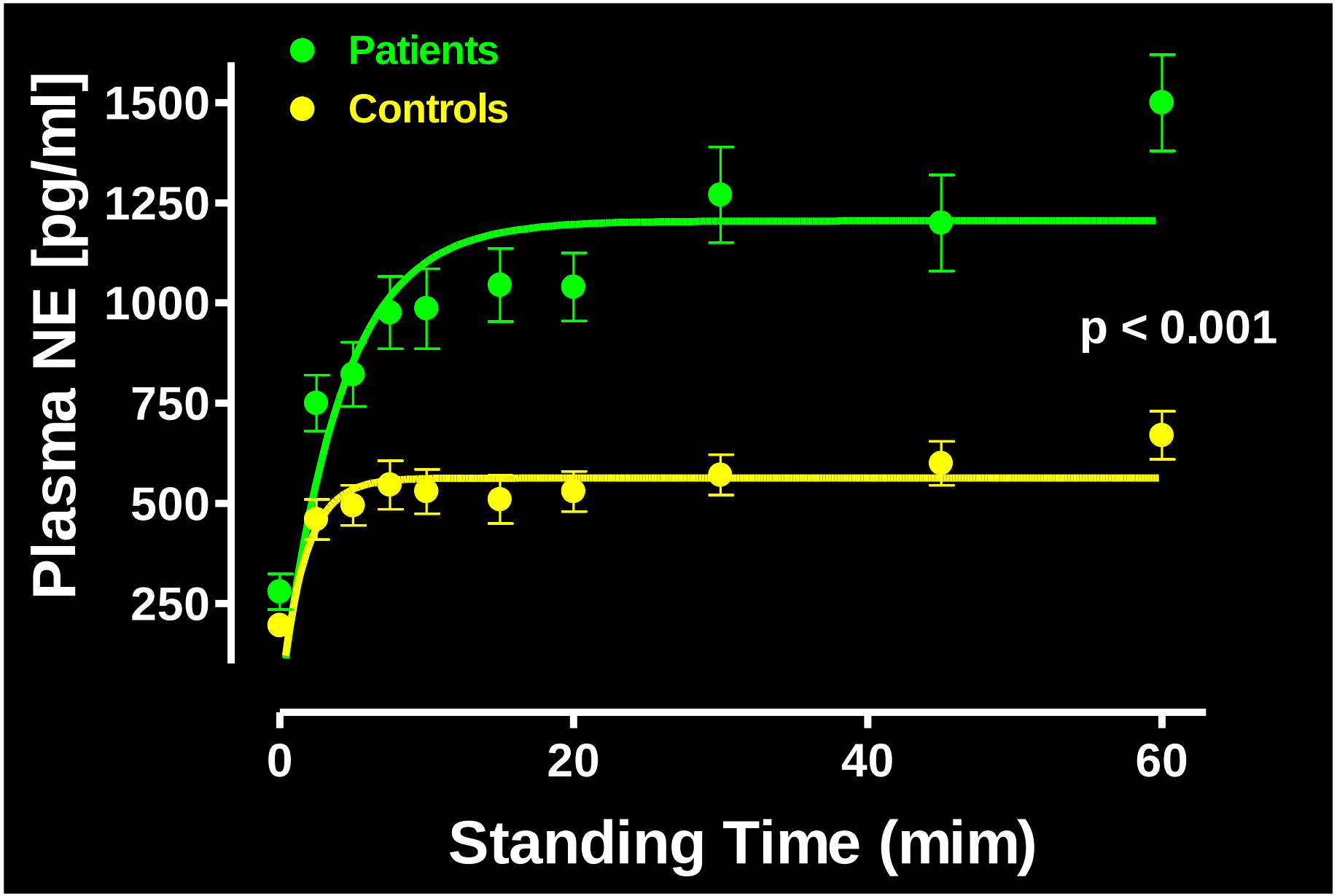
Epidemiology of POTS:

- Affects women >> men, 4-5:1
- Age 15-50 years
- Estimation: 0.5-1% of the population are affected ?
- Appears after: viral infection (EBV?), trauma, delivery, prolonged surgery, anecdotal causes, mostly unknown cause.
- Under-diagnosed, often symptoms are cyclic
- Usually is not a progressive illness and relief with aging
- A frequent cause of disability (social security, USA)

Pathophysiology of POTS:

- Hyperadrenergic, central high sympathetic tone (BP fluctuations..)
  - High circulating catecholamine
  - No evidence for neuropathy
- Neuropathic POTS (Partial loss of lower leg sympathetic nerves)
  - Leg's Blood Pooling – low end diastolic volume – sympathetic activation
  - Small Fiber Syndrome, high prevalence
- Idiopathic Hypovolemia (Renin-Angiotensin-Aldosetrone System)
- Blood volume re-distribution (toward mesenteric circulation)
- Autoimmune neuropathy

Norepinephrine



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Secondary POTS:

- Deconditioning very frequent and reversible with reconditioning
- Autoimmune and rheumatic diseases, Sjogren, SLE, APS, Sarcoidosis
- Diabetic Neuropathy (vagal neuropathy)
- Norepinephrine Transporter (NET) mutation, rare
- Syringomyelia and other neuropathies
- Mastocytosis (high histamine)
- Nuroendocrine tumors
- Spinal stenosis? , Chiari malformation
- Drugs, mainly psychiatric medications

Misdiagnosed POTS:

"enormous unmeasured source of preventable, morbidity and costs”

- Psychiatric illnesses, anxiety, depression, panic attacks, malingering, looking for attention …
- Supraventricular Tachycardia (SVT)
- Inappropriate Sinus Tachycardia (IST)
- Endocrine disorders, pheochromocytoma, carcinoid etc.
- Chronic Fatigue Syndrome (CFS), 15%, ….. IBS …..
- Fibromyalgia Syndrome (FMS), 10-20%
- Joint Hypermobility Syndrome = JHS (25% have POTS)

Hypermobility Syndrome: (~EDS-HT)

- Benign, to differentiate from Marfan's and other EDS
- = Ehler-Danlos Syndrome III (hypermobile type = HT)
- 2-30% in different populations
- High prevalence in Asian, Africans, Middle Eastern
- Females > Males
- Neuropathy, proprioceptive type
- Dysautonomia (POTS) is much more disabling

Gazit et al, Am J Med. 2003 Jul;115(1):33-40.

- ***Diagnosis***: Beighton score and Brighton criteria

Beighton score

Give yourself 1 point for each of the manoeuvres you can do, up to a maximum of 9 points

Ehlers-Danlos Support UK

Registered Charity 1157027

Can you bend your thumb back onto the front of your forearm?

left thumb 1 point

right thumb 1 point

Can you put your hands flat on the floor with your knees straight?

1 point

left hand 1 point

right hand 1 point

Can you bend your little finger up at 90º (right angles) to the back of your hand?

Can you bend your knee backwards?

left knee 1 point

right knee 1 point

Can you bend your elbow backwards?

right arm 1 point

left arm 1 point

www.ehlers-danlos.org
T: 020 8736 5604

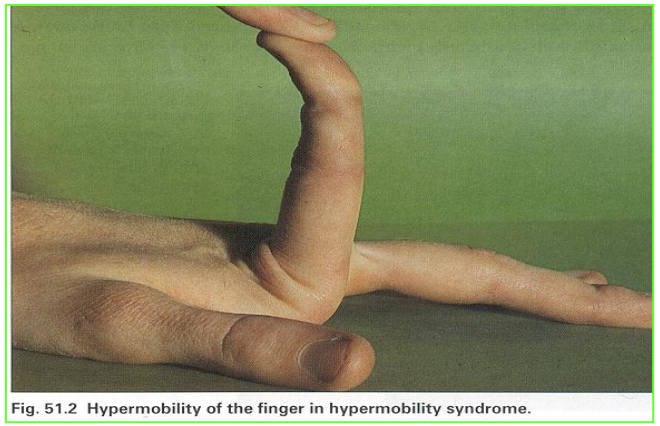


Fig. 51.2 Hypermobility of the finger in hypermobility syndrome.

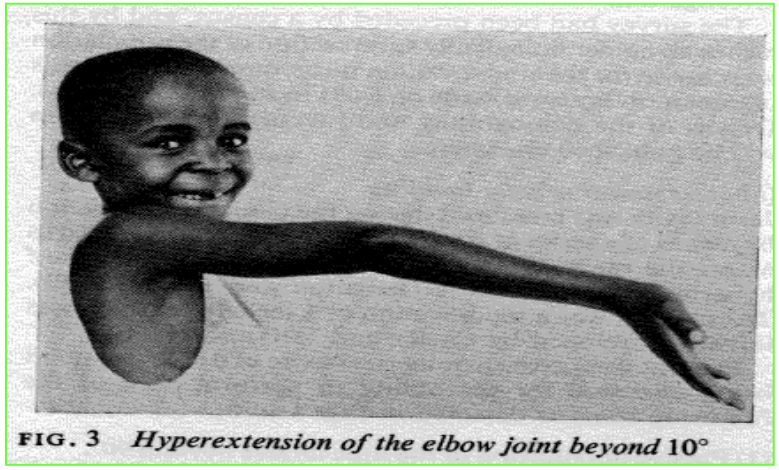


FIG. 3 *Hyperextension of the elbow joint beyond* 10°

Brighton criteria

Major criteria

Beighton score ≥ 4

Arthralgia in ≥ 4 joints

Minor criteria

Beighton score 1-3

Arthralgia in 1-3 joints

Back pain

Dislocating/Subluxating

Marfanoid Habitus

Thin, stretchy skin

Droopy eyelids

Varicose Veins

Hernia

Rectal or uterine prolapse

Workup for POTS

- Medical History, mostly diagnostic
- Physical examination: ΔHR > 30, BP no drop with standing
- ECG, normal: No need for stress test, Echocardiogram etc..
- Autonomic function tests, sweat tests, nerve biopsy (SFN)
- Blood sample for:
  - Thyroid function
  - B12
  - Basic function, kidney and Liver
  - CBC, Ferritin, Ferrum
  - Catecholamines, only in autonomic dysfunction centers

Quality of Life and Disability

- Some patients have cyclic and mild symptoms and can continue with normal daily life and work.
- For others, symptoms may be so severe that normal life is limited.
- Functional impairment seen in POTS patients is similar to that seen in chronic obsructive pulmonary disease (COPD) or congestive heart failure .
- Quality-of-life in POTS patients is comparable to patients with ESRD on dialysis.
- **Occupation**: misdiagnosed and under-diagnosed
- Approximately 25% of POTS patients are disabled and unable to work.

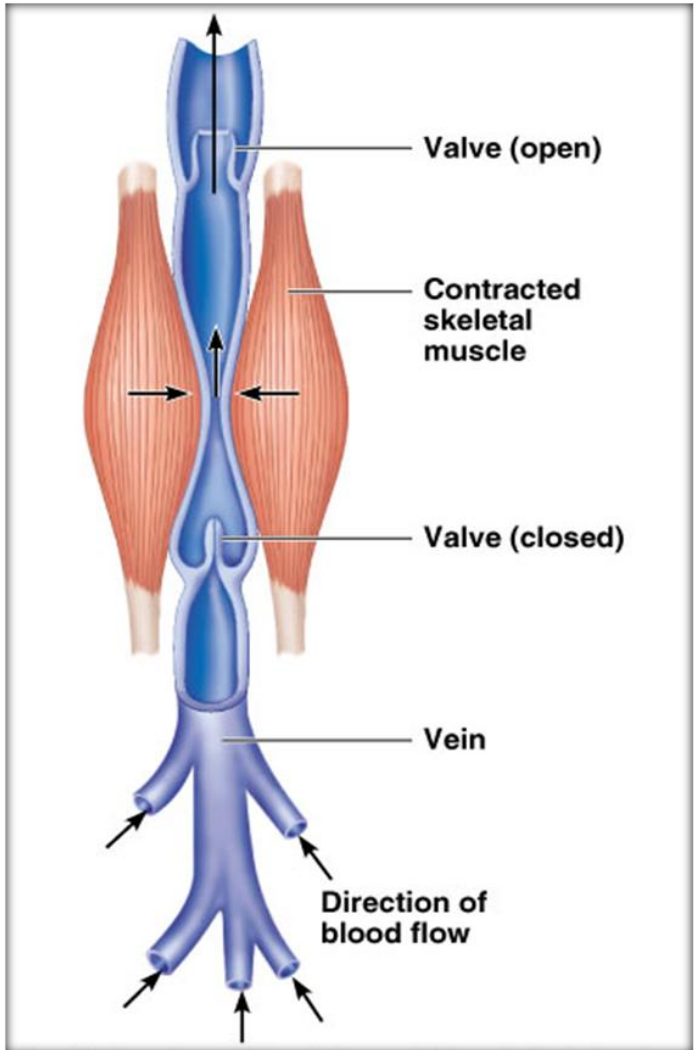
Management: Pharmacologic and non-pharmacologic

- Reassurance (diagnosis is a relieve)
- Exercise: needs long support plan, muscle strengthening of lower extremities, swimming ..
- Increase water drinking
- High salt diet
- Avoid energetic beverages and stimulants
- Small meals and without high carbohydrates
- Avoid prolong standing and upright working
- Biofeedback?

Movement of Blood Through Vessels

- Veins use the milking action of muscles to help move blood

"Second Heart"



Management: Pharmacologic and non-pharmacologic

- Reassurance (diagnosis is a relieve)
- Exercise: need long support plan, muscle strengthening of lower extremities, swimming ..
- Increase water drinking
- High salt diet, salt tablets, licorice roots
- Avoid energetic beverages and stimulants
- Small meals and low carbohydrates
- Avoid prolong standing and working setting
- Biofeedback?

Management: (2)

- Neuropathic POTS:
  - Peripheral vasoconstrictors (alpha-AR agonist, midodrine)
  - Pyridostigmine
  - Beta-blockers, propranolol the lower the dose is better
  - Volume expander: Fludrocortisone, erythropoietin, (& IV 0.9 saline)
- Hyperadrenergic (central ?)
  - Beta blockers, higher dose if not-tolerated, +/- Ivabradine
  - Centrally acting drugs, SSRIs and SNRI some of them
  - The above approach, also could be used after failure
- Unknown pathophysiology: (the majority..?)
  - Beta blockers and then proceed according to the response

“I don’t know, doesn’t mean not exist”

Thanks